Journal of the American College of Cardiology Vol. 58, No. 17, 2011

Published by Elsevier Inc.
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.05.059

EDITORIAL COMMENT

Are Coronary Plaque Characteristics on Computed Tomography Angiography Associated With Myocardial Perfusion?*

Juhani Knuuti, MD

Turku, Finland

Noninvasive quantification of myocardial perfusion in absolute terms has gained increasing interest recently. Although the technique has been available for 2 decades, only lately quantification has become feasible in clinical routine. This has been facilitated by wider clinical use of positron emission tomography (PET) in cardiac patients and the technical development of imaging cameras and software.

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The detection of functional consequences of epicardial coronary artery disease (CAD) has an established role in guiding the therapy of the disease (1). The traditional assessment of myocardial perfusion has been based on its relative distribution. This approach has obvious limitations because the interpretation is based on the assumption that the best perfused region is normal and can be used as a reference.

Measuring myocardial perfusion in quantitative terms is expected to provide benefits in several clinical scenarios (2,3). In multivessel disease, myocardial perfusion reserve may be variably abnormal in all territories, thereby reducing the heterogeneity of perfusion between "normal" and "abnormal" zones. An extreme case of multivessel disease is diffuse CAD or balanced disease in which perfusion is abnormally low in all myocardial regions. Typically, in relative analysis of perfusion, the images look homogeneous and the disease can be completely missed if no other signs of multivessel disease are evident. In addition, the assessment of impairment in microcirculatory reactivity has recently gained more attention. Estimates of myocardial perfusion contain independent prognostic information about future major cardiac events and perfusion assessment is also useful in the monitoring of the effectiveness of risk reduction strategies (1).

Cardiac computed tomography (CT) enables visualization of coronary stenoses, and several studies have demonstrated a high negative predictive value for CAD (4). Although contrast-enhanced CT is able to assess coronary artery lumen, there is often discrepancy between anatomy and myocardial blood supply. In addition to technical limitations of CT, the vasomotor tone and coronary collateral flow cannot be estimated because the degree of stenosis is only a weak descriptor of coronary resistance. In accord with this, only about half of the anatomically significant lesions detected with CT coronary angiography are flow limiting (5). The unique feature of CT angiography is that it allows characterization of coronary plaque morphology and composition as well as vessel remodeling, and these have been believed to provide additional prognostic information. However, the clinical value of these findings is not yet clear.

The paper by Naya et al. (6) in this issue of the *Journal* focused on this topic and assessed the link between coronary atherosclerosis morphology detected by CT angiography and myocardial perfusion and perfusion reserve as measured in absolute terms using PET and rubidium-82. The atherosclerosis plaque burden, morphology, and composition were carefully analyzed in 73 consecutive patients using current standard CT. Regional and global myocardial perfusion was quantified at rest and during pharmacologic hyperemia.

As expected, the authors found that global quantitative estimates of myocardial perfusion parameters were sensitive markers for the identification of patients with high-risk anatomic disease by CT angiography. Also, in agreement with earlier findings, they found only a modest relationship between the degree of stenosis severity by CTA and its downstream effect on myocardial perfusion parameters such as hyperemic perfusion, perfusion reserve, and coronary vascular resistance as assessed per vessel region. Interestingly, total plaque length, composition, and remodeling index were not associated with perfusion parameters. On the other hand, on a per-patient basis, the modified Duke CAD index and the number of segments with mixed plaque composition were the best predictors of low global perfusion reserve.

These results suggest that CT angiography–based descriptors of coronary atherosclerosis do not add incremental information beyond the quantitative percentage of diameter stenosis for predicting impaired tissue perfusion. However, this does not necessarily mean that these CTA descriptors would not provide incremental prognostic value over myocardial perfusion because this study was not designed to

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology. Dr. Knuuti has reported that he has no relationships relevant to the contents of this paper to disclose.

From the Turku PET Centre, University of Turku and Turku University Hospital, Turku, Finland.

study that. This question needs to be studied in a larger study with follow-up. However, the extent of atherosclerosis was associated with decreased tissue perfusion, suggesting a link between noncalcified plaques as a surrogate marker of more diffuse coronary microvascular dysfunction.

Interestingly but not surprisingly, Naya et al. (6) detected quite widespread physiologic variability in perfusion parameters, even in coronary territories supplied by angiographically normal vessels or those with nonobstructive disease. This is a known phenomenon from numerous studies linking abnormal perfusion reserve with risk factors for CAD such as hyperlipidemia, hypertension, and diabetes. Based on this study, the quantitative assessment of perfusion would be a very sensitive but not a specific marker for obstructive epicardial CAD. However, this does not exclude that low myocardial perfusion may have prognostic value beyond the diagnosis of CAD.

In our recent study with quantification of myocardial perfusion, we also found a small number of patients (6%) who had low absolute stress perfusion without epicardial CAD (2). However, in that study, the perfusion in nonstenosed vessel regions in patients with significant stenoses elsewhere was not commonly reduced and did not cause noteworthy problems in assessing the functional severity of CAD. The difference between the results of the Naya et al. (6) study and our study may be attributed to differences in patient populations. In patients with more advanced CAD, the likelihood of diffuse atherosclerosis and the vascular damage caused by risk factors is likely higher. The patients in the study by Naya et al. had apparently more risk factors and generally more severe atherosclerosis. Different perfusion tracers were used in these studies, and this could have played some role, although quantification using rubidium-82 has been also quite well validated.

One of the main limitations of this study, in addition to a rather small population of patients with significant CAD, was the lack of a reference standard for both anatomic and functional parameters. CT angiography is known to overestimate stenoses. Also, CT angiography cannot exclude that the reduction of perfusion in vessels with nonsignificant stenoses was not due to coronary artery disease. A larger cohort with invasive measurements needs to be studied prospectively to better understand the relationship between perfusion parameters and coronary atherosclerosis. Also, the study could not analyze the power of combined data (hybrid imaging) from CT angiography and perfusion imaging for the diagnosis of CAD due to lack of a reference standard.

Reprint requests and correspondence: Dr. Juhani Knuuti, Turku PET Centre, University of Turku, P.O. Box 52, Turku FIN-20521, Finland. E-mail: juhani.knuuti@utu.fi.

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Key Words: atherosclerosis ■ coronary computed tomography angiography ■ myocardial flow reserve ■ plaque morphology ■ positron emission tomography.